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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/517,466	03/02/2000	James L. Hartley	IVGN 223	4289

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EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
09/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/517,466	HARTLEY ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 13, 2007 has been entered. It is also noted that the amendment to the specification filed September 24, 2007 has now been entered, and that the remarks of September 24, 2007 have been considered.

2. Claim 39 has been amended, and claims 50-56 have been canceled. Claims 39-49 are now pending and under consideration.

Claim Rejections - 35 USC § 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 39-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

Independent claim 39 has been amended to include the limitation "wherein the nucleotide sequence is located within an *att* recombination site which is capable of undergoing recombination with a cognate *att* site containing the same nucleotide sequence." The remarks of September 24, 2007 indicate that support for this amendment may be found at page 59, line 22 through page 61, line 7 of the specification. However, while this portion of the specification discloses recombination sites including mutated core regions, there is no apparent support for "cognate att sites" containing the same sequence or for recombination between "an att recombination site" and a "cognate att site" having such a mutated core sequence, as recited in the amended claims. Further, support for this limitation is not found elsewhere in the originally filed specification or claims. Accordingly, applicants' amendment introduces new matter.

5. Claims 39-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid molecules comprising SEQ ID NO: 87 (including the molecule disclosed by applicant as SEQ ID NO: 60), does not reasonably provide enablement for any isolated nucleic acid molecule comprising the nucleotide sequence of (a) of claim 39 located "within an *att* recombination site which is capable of undergoing recombination with a cognate *att* site containing the same nucleotide sequence." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The claims are to drawn isolated nucleic acid molecules comprising the nucleotide sequence ATTATAC located "within an *att* recombination site which is capable of undergoing recombination with a cognate *att* site containing the same nucleotide sequence," as well as various vectors and host cells comprising the nucleic acid molecule. Thus, the claims require a molecule comprising any *att* recombination site having within it at any location the sequence ATTATAC, where the *att* recombination site "is capable of undergoing recombination with a cognate *att* site containing the same nucleotide sequence" (i.e., containing ATTATAC).

It is unpredictable as to whether one of skill in the art could make and use applicant's invention in a manner reasonably commensurate with the claims. The specification provides evidence that the mutation of the first nucleotide of the 7 base pair overlap of the attL recombination site 15 base pair core region from T to A (such that the 7 base pair sequence changes from TTTATAC to ATTATAC) results in

increased recombination efficiency (see Examples 21 and 22, and SEQ ID Nos 60 and 87 in particular). Accordingly, one of skill in the art could clearly prepare nucleic acids comprising such mutated attL sequences and use said nucleic acids in various methods requiring site-specific recombination. However, the specification is silent with regard to other *att* recombination sites comprising this particular mutated sequence, and with regard to what effect this mutation would have (if any) on recombination using such sequences. Further, the specification does not disclose the use of molecules comprising this 7 base pair sequence located at any other location within the attL recombination site; rather, the specification establishes the effectiveness of a specific mutation at a specific location in increasing recombination efficiency. Thus, while the specification enables the use of one particular type of nucleic acid molecule encompassed by the claims, the vast majority of molecules encompassed by the instant claims are not enabled by the teachings of applicant's specification. Given the high level of skill of one skilled in the relevant art, it is clearly within the ability of such a practitioner to synthesize a variety of molecules encompassed by the claims and to, e.g., assay those molecules to determine whether any of them are useful in recombination. However, the outcome of such experimentation cannot be predicted, and therefore it is completely unpredictable as to whether such additional molecules could be successfully used in a manner analogous to the particular attL mutant sequence employed by applicant. Lacking guidance from the specification, one skilled in the art may look to the teachings of the prior art for further guidance and enablement of a claimed invention. However, in the instant case, the prior art does not disclose

other molecules meeting the requirements of the claims. The closest prior art reference, Zucman-Rossi et al (Proc. Natl. Acad. Sci. USA 95:11786-11791 [9/1998]) discloses a sequence comprising a breakpoint region (EWSR1) that includes the sequence ATTATAC (see entire reference, particular page 11786 and Figure 1, as well as the sequence disclosed in GenBank Accession No. Y08806, in which ATTATAC is located, e.g., within intron 8 at nucleotide 38969). However, the sequence ATTATAC in the molecule of Zucman-Rossi et al is not located within a "recombination site" as required by the instant claims – the site flanking ATTATAC in the molecule does not correspond to that of a known recombination site, and Zucman-Rossi et al do not disclose that this particular site is a breakpoint or that recombination proteins bind this site, etc. Accordingly, the teachings of the prior art cannot be relied upon for enablement of additional molecules encompassed by applicant's claims. Thus, given the lack of sufficient guidance provided by the specification and the prior art, it would require undue experimentation to make and use applicant's invention in a manner reasonably commensurate with the instant claims.

It is noted that applicants' remarks of September 24, 2007 regarding the prior rejection of the claims for lack of enablement have been considered. However, applicants' arguments appear to pertain to att recombination sites that include the sequence ATTATAC that have the capability of "undergoing recombination with a cognate att site containing the same nucleotide sequence" (i.e., that include ATTATAC), whereas applicants' claims as written require this capability of the recited "att recombination site" itself (as opposed to a site actually including ATTATAC). Thus,

applicants' arguments are moot with regard to the claims as amended, which claims lack enablement and include new matter as described above. Thus, applicants' arguments are not persuasive.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634

Diana B. Johannsen
Primary Examiner
Art Unit 1634